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Candidate herbal medicines with antiviral activity against covid 19

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Abstract
Coronavirus disease (COVID-19), is an extremely infectious disease. Since 2019, a terrible pandemic of this disease has swept the globe, and it hasn't stopped, with regular mutations transforming into aggressive and contagious versions. As the world struggles with coronavirus infection, patients are being treated with a variety of antiviral medications and symptomatic therapies, and clinical trials are in progress. In these circumstances, it is more important to consider all of the treatment options for COVID-19, including herbal medicine. People reckon that the COVID-19 patient would be relieved from symptoms and cured by using herbal immunomodulators. In many countries, herbal medication has already been used to manage corona such as China, Africa, Iran. On account of not having adequate preclinical and clinical studies regarding the effect of herbal medication on coronavirus, some herbal medicine plants could be effective to treat patients based on the previous experiments. Some herbal medicines, such as Curcuma longa, Garlic, Cinchona, Echinacea, Ginger, and Curcuma xanthorrhiza are discussed in this article as effective treatments for COVID-19 due to their antiviral effects. Although their effectiveness is still controversial and further research is needed, we also review some impacts of herbal and draw conclusions at the end of the session.

Keywords: COVID-19, Herbal, Curcuma, Garlic, Cinchona, Echinacea, Ginger, Xanthoriza

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1. Introduction

Coronavirus disease (COVID-19) is caused by a coronavirus that causes infection among people all around the world, ranging from a flu-like syndrome to severe health-related problems.[1] COVID-19 was diagnosed first in December 2019, and the World Health Organization (WHO) it a pandemic in March 2020. [2] There have been more than 178,700 confirmed patients in at least 140 countries as of March 2020. The number of cases was documented in mainland China, with Italy, Iran, Spain, and South Korea following closely behind. [3] As of February 15, 2022, there have been 408 910 752 documented cases of COVID-19 and 5 802 226 deaths have been announced worldwide (Figure 1). [4]

COVID-19 has common symptoms such as fever, fatigue, shortness of breath, and cough. In Serious cases, pneumonia and organ failure may occur and lead to even death. [5] After exposure to transmissible sources including droplets, direct contact, aerosol, droplets fomites, animal-human, and fecal-oral transmission, SARS-CoV-2 has an incubation period of 2–14 days. The initial stage of the infection might be asymptomatic or characterized by lower and upper respiratory tract infection (RTI) symptoms, such as typical symptoms, and closely correlated with smell and taste disorders or with gastrointestinal problems. 7 to 10 days after the beginning of symptoms, some patients may experience a rapid clinical deterioration, marked by respiratory symptoms which may be linked with thromboembolic complications. Finally, a subsequent step in the acute development of SARS-CoV-2 has been recognized as acute respiratory disease. [6]

There are no available specific medicines as an effective treatment of COVID-19 Currently. During this COVID-19 pandemic, different treatment approaches have been asserted, including herbal and traditional medicine, which has been used as an antiviral medication against some viruses such as H1N1 influenza. [7] Consumption of herbal containing active chemicals with antibacterial, immunostimulatory, antiviral, and anti-inflammatory effects, such as curcumin, echinacea, and quinine, is a new trend in society. These herbal substances are thought to have the ability to modify immune responses, and hence to have therapeutic effects in treating and preventing COVID-19. [8, 9] This article explains that herbal medication may have antiviral effects to treat the COVID-19 as a non-viral medication.

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Figure 1:WHO Weekly operational update on COVID-19

2. Candidate herbal medicines

Herbal medicines are often used by many individuals in the community in this circumstance, when preventative and therapeutic agents have not been established and approved for administration to patients. As explained previously, we conducted a review of multiple publications from various journals. At least six herbals have been identified as having the potential to prevent or the treatment of COVID-19 patients due to having antiviral and other beneficial effects.

2.1. Curcumin longa

Curcumin (Figure 2) is extracted from roots of rhizome.people are known it as Curcuma longa (C. longa).This plant is used in science and medicen.Turmeric is a member of the ginger family.In Asian, C. longa is used as a medicine against several diseases(such as inflammatory bowel disease(IBD), diabetes mellitus, psoriasis, asthma, neurodegenerative disease, obesity, cardiovascular disease, and allergy), due to having anti-cancer, anti-inflammation, and antioxidant effects.[10, 11].

Curcumin has antiviral properties against a wide range of viruses such as influenza, HIV, HSV-2, hepatitis virus, adenovirus Zika virus, and HPV. [12,13] Other studies revealed that curcumin has had immunostimulatory impacts (by increasing tumor necrosis factor (TNF-α) and IL-6) as well as anti-inflammatory effects (by decreasing TNF-α, phosphatidylinositol-3 kinase (PI3K), nuclear factor-kappa B (NF-κB), and IL-6). [14-16]

In many hospitalized patients in India, nutritional supplementation of curcumin with zinc and vitamin C has shown promising benefits in strengthening natural immunity and preventive defense against infections. It's also reported that curcumin's pharmacological formulation in a nanoemulsion system resulted in increasing bioavailability and solubility as well as a stronger antihypertensive impact. [17] Some studies have reported that curcumin has a long-term (more than 3 months) antihypertensive effect. [18] Increasing the level of angiotensin-converting enzyme (ACE) is one reason for hypertension and ACE inhibitor is one mechanism to control high blood pressure. According to the studies, COVID-19

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patients have hypertension as usual comorbidity and Curcumin works as an ACE inhibitor. So, Curcumin may be efficient in controlling hypertension in COVID-19 patients. [19-21].



Figure 2 : Curcumin longa



Figure 3: Garlic



Figure 4: Cinchona

2.2. Garlic

Garlic (Allium sativum) (Figure 3) contains phytochemicals like sulfur which have positive effects such as immunosuppressor, anticancer, cardioprotective, anti-inflammatory, and anti-inflammatory. [22] Garlic has been used as a food and flavoring herb for thousands of years, as well as a traditional treatment for a variety of ailments, such as viral disorders. [23, 24] The antiviral effects of garlic against HIV, Influenza B, a gammaretrovirus, herpes simplex virus, and coxsackievirus species were revealed. [25] Khubber et al. claimed that adding garlic and its products into a daily diet can be effective as adjuvant therapy and may improve the toxicity and side effects of the main medication. Furthermore, garlic can decrease the rate of infection due to SARS- CoV-2. SO, it has a beneficial role in the incidence decline of COVID-19 in various communities.[26] Another study reported that garlic is beneficial for respiratory diseases such as bronchitis infection due to coronavirus and influenza and improves the immune system. [27]

2.3. Cinchona

Cinchona trees were discovered to heal fever first. Then people found that the bark of these trees (Figure 4) might be beneficial as a cure for malaria which is called quinine. The anti-malaria effect of quinine is the same as chloroquine. [28, 29] Some studies revealed that chloroquine could use as an antiviral for SARS-CoV infection. Therefore, quinine (chloroquine analog) might show positive effects on COVID-19 patients. [30, 31]

Baroni et al reported that quinine had an antiviral effect by several process such as inhibiting NF-kB, running the protein heat shock response, and blocking virus replication.[32] Quinine has an antiviral activity that suppresses both the immune system and antiviral activity. If quinine increases IFN-α cytokine levels, it acts as an immune stimulant. In contrast, if quinine reduces TNF-α levels by inhibiting release, it is known as an immunosuppressant. Although both of these activities can have positive effects on patients with Covid-19, some studies recommended not to use of quinine routinely.[33]

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2.4. Echinacea

Echinacea (Figure 6) species especially Echinacea purpurea (E. purpurea), one of the most popular clinically studied herbal medicines in part of North America and Europe and for this reason reveals promising impacts as a treatment for viral infections.[34]Earlier research revealed that Echinacea might decline the severity and duration of respiratory infections. [35]

Although some studies announced that it had significant antiviral effect, other impacts on immune system and inflammation are still controversial. Sharma et al. reported that echinacea extract could be used as an herbal antiviral treatment for the enveloped virus such as influenza and herpes simplex virus and less impact on naked virus including adenoviruses and rhinoviruses.

According to this report, E. purpurea can be used as an effective treatment against coronavirus as a membrane virus. [36] Some production containing echinacea assert that they act as an immunostimulatory and not as an an immunosuppressor. Burger et al. reported that echinacea may increase the release of several cytokines from macrophages such as IL-1, IL-10 and TNF-α. [37] Macrophages can phagocytose SARS-CoV-2 and release TNF-α with other cytokines. [38]



Figure 5 : Ginger



Figure 6: Echinacea



Figure 7: Curcuma xanthorrhiza

2.5. Ginger

Ginger (Figure 5) has numerous therapeutic usages, such as anticancer, antioxidative, antimicrobial, anti-inflammatory, anti-fungal, hepatoprotective, hypo-cholesterolemic, immunomodulatory, antimigraine, antidiabetic, anti-nausea, cardioprotective, anti-obesity, neuroprotective, anti-emetic, and respiratory protective effects. [39]

Fresh ginger has antiviral effects against viruses such as rhinovirus and human respiratory syncytial virus (HRSV).

And also, it is more beneficial to treat airway infection due to viruses.Before inoculation of HRSV(1-2 hours), The extract of ginger can inhibit the virus attaching to cells of epidermoid carcinoma or lung carcinoma.

Stimulating the release of interferon α and β from the epithelial cell is another effect of ginger to inhibit spreading viruses to the lower-respiratory tract.[40]

After dehydration or cooking ginger, shogaol is produced. Shogaol has anticancer, antiemetic, antioxidant, neuroprotective, and anti-inflammatory impacts. Paradol is synthesized from shogaol and exhibits anti-inflammatory, anticancer, neuroprotective, and cardioprotective effects.[41, 42]

Zingerone which is produced from drying and heating or roasting the ginger, has enormous benefits, including antispasmodic, antidiabetic, anxiolytic, anticancer, antimicrobial, protection from radiation,anti-hyperlipidemia, anti-inflammatory, anti-oxidant, antimicrobial, antiemetic, and antidiarrheic effects.[43]

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According to different studies, the cover 19 patient who consumed ginger with or without main treatment, had fewer symptoms especially coughing, muscular pain, and breath shortness(in Bangladesh, Tunis, and Iran studies). [44-46]
Moreover, the rate of hospitalization for getting treatment for COVID 19 was lower among the patients consuming ginger (In Saudi Arabia and Iran studies). [47-48] In Africa, ginger mixes with other herbal plants to use as a treatment for COVID-19. [49]

2.6. Curcuma xanthorrhiza

Xanthorrhizol (XNT) (Figure 7) or Curcuma xanthorrhiza Roxb (C. xanthorrhiza) is used in Asian countries as an herbal plant. [50] C. xanthorrhiza (Curcuma Zedoaria) has some beneicial impacts such as an antioxidant, antihypertensive, anti-inflammatory, anticancer, antimicrobial, antiplatelet, nephroprotective, antihyperglycemic, and useful for systemic diseases like systemic lupus erythematosus (SLE). [51-54]
The study regarding xanthorrhizol revealed that this compound decline inflammatory genes in the liver, muscle, and adipose tissue in diabetes mellitus patients. And also, it can inhibit the production of inflammatory cytokine and the expression of tumor necrosis factor (TNF-α) and interleukin (IL-1β). [55]
Singgih Wahono et al. reported that xanthorrhiza is able to decline the level of IL-6 as well as raise serum transforming growth factor (TGF-β) in patients diagnosed with SLE. [56]
Another study claim that Xanthorrhizol can be used as an immunosuppressant for COVID-19. Owing to inhibiting proinflammatory cytokines. However, it needs further investigations before recommending xanthorrhizol for prevention and treatment in COVID-19 patients. [57]

3.Conclusion

This review suggests that these selected herbal medicines may have the ability to regulate the synthesis and secretion of cytokines, interfere with the virus's growth in host cells, and have antiviral effects, according to the preceding explanation. Herbal medication might be effective in the battle against. Herbal agents might be effective in the battle against COVID-19. Furthermore, patients should be advised that using supplements with one of these chemicals to prevent COVID-19 or treat the illness without particular advice or under the direct supervision of a doctor or a specialist is still not suggested. A recommendation for the clinician is that patients should be prescribed these herbal remedies carefully, even if they do not have any illnesses owing to the debate regarding this information. Moreover, Further research is needed on the antiviral effects of herbal medicines against COVID-19.

Available information

This information in this article comes from previously published research and datasets that have been referenced.

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References

[1] Centers for Disease Control and Prevention (CDC). Coronavirus Disease 2019 (COVID-19) situation summary; 2020. Available from: https://www.cdc.gov/ coronavirus/2019-nCoV/summary.html. Accessed March 6, 2020.
[2] World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020; 2020. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks- at-the-media-briefing-on-covid-19 – 11-march-2020. Accessed March 11, 2020.
[3] Lai KKR, Wu J, Harris R, McCann A, Collins K, Watkins D, et al. Coronavirus map: tracking the spread of the outbreak; 2020. Available from: https://www.nytimes.com/interactive/2020/world/coronavirus-maps. html?action=click&module=RelatedLinks&pgtype=Article. Accessed March 17, 2020
[4] World Health Oragnization (2022) Coronavirus disease (COVID-2019) situation report. [Accessed: 15/02/2022], https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---15-february-2022
[5] World Health Organization (WHO). Q&A on coronaviruses (COVID-19); 2020. Available from: https://www.who.int/news-room/q-a-detail/q-a- coronaviruses. Accessed March 6, 2020
[6] Gautret P, Million M, Jarrot PA, Camoin-Jau L, Colson P, Fenollar F et al (2020) Natural history of COVID19 and therapeutic options. Expert Rev Clin Immunol. 16:1159 84. https://doi.org/10.1080/1744666X.2021.1847640
[7] Luo H, Tang QL, Shang YX, Liang SB, Yang M, Robinson N, et al. Can Chinese medicine be used for prevention of corona virus disease 2019 (COVID-19)? A review of historical classics, research evidence and current prevention pro- grams. Chinese J Integr Med 2020, http://dx.doi.org/10.1007/s11655-020-3192-6
[8] M. Sharma, S. A. Anderson, R. Schoop, and J. B. Hudson, "Induction of multiple pro-inflammatory cytokines by re- spiratory viruses and reversal by standardized Echinacea, a potent antiviral herbal extract," Antiviral Research, vol. 83, no. 2, pp. 165–170, 2009.
[9] B. Kocaadam and N. S ¸anlier, "Curcumin, an active compo- nent of turmeric (Curcuma longa), and its effects on health," Critical Reviews in Food Science and Nutrition, vol. 57, no. 13, pp. 2889–2895, 2017.
[10] B. Kocaadam and N. S ¸anlier, "Curcumin, an active compo- nent of turmeric (Curcuma longa), and its effects on health," Critical Reviews in Food Science and Nutrition, vol. 57, no. 13, pp. 2889–2895, 2017.
[11] S. Hewlings and D. Kalman, "Curcumin: a review of its' effects on human health," Foods, vol. 6, no. 92, pp. 1–11, 2017. 9-B. Kocaadam and N. Şanlier, "Curcumin, an active component of turmeric (Curcuma longa), and its effects on health," Critical Reviews in Food Science and Nutrition, vol. 57, no. 13, pp. 2889–2895, 2017.
[12] Das S, Sarmah S, Lyndem S, Roy AS. An investigation into the identification of potential inhibitors of SARS-CoV-2 main protease using molecular docking study. J Biomol Struct Dyn. 2020;13:1–11.
[13] Praditya D, Kirchhoff L, Brüning J, Rachmawati H, Steinmann J, Steinmann E. Anti-infective properties of the golden spice curcumin. Front Microbiol. 2019;10:912.

www.SID.ir

[14] M. Catanzaro, E. Corsini, M. Rosini, M. Racchi, and C. Lanni, "Immunomodulators inspired by nature: a review on curcumin and Echinacea," Molecules, vol. 23, no. 2778, pp. 1–17, 2018.
[15] K. Shimizu, M. Funamoto, Y. Sunagawa et al., "Anti-inflammatory action of curcumin and its use in the treatment of lifestyle-related diseases," European Cardiology Review, vol. 14, no. 2, pp. 117–122, 2019.
[16] R. M. Shimizu, S. Singh, S. K. Dubey, K. Misra, and A. Khar, "Immunomodulatory and therapeutic activity of curcumin," International Immunopharmacology, vol. 11, no. 3, pp. 331–341, 2011.
[17] Rachmawati H, Soraya IS, Kurniati NS, Rahma A. In vitro study on antihypertensive and antihypercholesterolemic effects of a curcumin nanoemulsion. Sci Pharm. 2016;84(1):131–40.
[18] A. Hadi, M. Pourmasoumi, E. Ghaedi, and A. Sahebkar, "The effect of Curcumin/Turmeric on blood pressure modulation: a systematic review and meta-analysis," Pharmacological Research, vol. 150, pp. 1–30, 2019.
[19] A. J. Akinyemi, I. A. Adedara, G. R. Thome et al., "Dietary supplementation of ginger and turmeric improves reproductive function in hypertensive male rats," Toxicology Reports, vol. 2, pp. 1357–1366, 2015.
[20] L. Fang, G. Karakiulakis, and M. Roth, "Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?" *The Lancet Respiratory Medicine*, vol. 8, no. 4, p. e21, 2020.
[21] F. Alhenc-Gelas, N. Bouby, and J.-P. Girolami, "Kallikrein/K1, kinins, and ACE/kininase II in homeostasis and in disease insight from human and experimental genetic studies, therapeutic implication," *Frontiers in Medicine*, vol. 6, pp. 1–13, 2019.
[22] El-Saber Batiha G, Magdy Beshbishy A, Wasef LG, Elewa YH, Al-Sagan AA, El- Hack A, et al. Chemical constituents and pharmacological activities of garlic (Allium sativum L.): A review. Nutrients. 2020;12(3):872. https://doi.org/10. 3390/nu12030872.
[23] E. Ayaz, H.C. Alpsoy, Garlic **(***Allium sativum***)** and traditional medicine, Turkiye Parazitoloji Dergisi, 31 (2)(2007), pp. 145-149
[24] R. Rehman, S. Saif, M.A. Hanif, M. Riaz, Medicinal plants of South Asia, Elsevier B. V, Amsterdam (2019) (Chapter 23) - Garlic
[25] Chakraborty D, Majumder A. Garlic (Lahsun)–an immunity booster against SARS-CoV-2. Biotica Res Today. 2020;2(8):755–7.
[26] Khubber, S., Hashemifesharaki, R., Mohammadi, M. *et al.* Garlic (*Allium sativum* L.): a potential unique therapeutic food rich in organosulfur and flavonoid compounds to fight with COVID-19. *Nutr J* 19, 124 (2020).
[27] Chattopadhyay, D, and Naik, T.N. (2007). Antivirals of ethnomedicinal origin: structure-activity relationship and scope. Mini reviews in medicinal chemistry7, 275-301.
[28] C. Maldonado, C. J. Barnes, C. Cornett et al., "Phylogeny predicts the quantity of antimalarial alkaloids within the iconic yellow *Cinchona* bark (Rubiaceae: *Cinchona calisaya*)," *Frontiers in Plant Science*, vol. 8, pp. 1–16, 2017.
[29] E. Abolghasemi, S. H. Moosa-Kazemi, M. Davoudi, A. Reisi, and M. T. Satvat, "Comparative study of chloroquine and quinine on malaria rodents and their effects on the mouse testis," *Asian Pacific Journal of Tropical Biomedicine*, vol. 2, no. 4, pp. 311–314, 2012.
[30] M. J. Vincent, E. Bergeron, S. Benjannet et al., "Chloroquine is a potent inhibitor of SARS coronavirus infection and spread," *Virology Journal*, vol. 2, no. 69, pp. 1–10, 2005.

www.SID.ir

[31] P. Gautret, J. C. Lagier, P. Parola et al., "Hydroxychloroquine and azithromycin as a treatment of COVID-19: result of an open label non-randomized clinical trial," *Journal of Antimicrobial Agents*, Article ID 105949, pp. 1–25, 2020.
[32] A. Baroni, I. Paoletti, E. Ruocco et al., "Antiviral effects of quinine sulfate on HSV-1 HaCat cells infected: analysis of the molecular mechanisms involved," *Journal of Dermatological Science*, vol. 47, no. 3, pp. 253–255, 2007.
[33] Rhea Veda Nugraha, Hastono Ridwansyah, Mohammad Ghozali, Astrid Feinisa Khairani, Nur Atik,"Traditional Herbal Medicine Candidates as Complementary Treatments for COVID-19: A Review of Their Mechanisms, Pros and Cons", Evidence-Based Complementary and Alternative Medicine, vol. 2020, Article ID 2560645, 12 pages, 2020.
[34] M. Sharma, S. A. Anderson, R. Schoop, and J. B. Hudson, "Induction of multiple pro-inflammatory cytokines by respiratory viruses and reversal by standardized Echinacea, a potent antiviral herbal extract," *Antiviral Research*, vol. 83, no. 2, pp. 165–170, 2009.
[35] S.S. Percival, Use of echinacea in medicine, Biochem Pharmacol, 60 (2) (2000), pp. 155-158
[36] M. Sharma, S. A. Anderson, R. Schoop, and J. B. Hudson, "Induction of multiple pro-inflammatory cytokines by respiratory viruses and reversal by standardized Echinacea, a potent antiviral herbal extract," *Antiviral Research*, vol. 83, no. 2, pp. 165–170, 2009.
[37] R. A. Burger, A. R. Torres, R. P. Warren, V. D. Caldwell, and B. G. Hughes, "Echinacea-induced cytokine production by human macrophages," *International Journal of Immunopharmacology*, vol. 19, no. 7, pp. 371–379, 1997.
[38] E. Prompetchara, C. Ketloy, and T. Palaga, "Immune responses in COVID-19 and potential vaccines: lessons learned from SARS and MERS epidemic," *Asian Pacific Journal of Allergy and Immunology*, vol. 38, no. 1, pp. 1–9, 2020.
[39] A. Jafarzadeh, M. Nemati, Therapeutic potentials of ginger for treatment of Multiple sclerosis: a review with emphasis on its immunomodulatory, anti-inflammatory and anti-oxidative properties, J Neuroimmunol, 324 (2018), pp. 54-75
[40] J.S. Chang, K.C. Wang, C.F. Yeh, D.E. Shieh, L.C. Chiang, Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines, J Ethnopharmacol, 145 (1) (2013), pp. 146-151
[41] X.R. Kou, X.Q. Wang, R. Ji, *et al.* Occurrence, biological activity and metabolism of 6-shogaol, Food Funct, 9 (3) (2018), pp. 1310-1327
[42] R. Kiyama, Nutritional implications of ginger: chemistry, biological activities and signaling pathways, J Nutr Biochem, 86 (2020), p. 108486
[43] J.G. Choi, S.Y. Kim, M.S. Jeong, M.S. Oh, Pharmacotherapeutic potential of ginger and its compounds in age-related neurological disorders, Pharmacol Ther, 182 (2018), pp. 56-69
[44] M.N. Azam, R. Al Mahamud, A. Hasan, R. Jahan, some home remedies used for treatment of COVID-19 in Bangladesh, J Med Plants Studies, 8 (4) (2020), pp.
[45] W.A. Wannes, M.S. Tounsi, Can medicinal plants contribute to the cure of Tunisian COVID-19 patients? J Med Plants Studies, 8 (5) (2020), pp.
[46] M. Mesri, S.S. Esmaeili Saber, M. Godazi, et al. The effects of combination of Zingiber officinale and Echinacea on alleviation of clinical symptoms and hospitalization rate of suspected COVID-19 outpatients: a randomized controlled trial, J Compl Integr Med (2021), 10.1515/jcim-2020-0283

www.SID.ir

[47] L.A. Aldwihi, S.I. Khan, F.F. Alamri, *et al.* Patients' behavior regarding dietary or herbal supplements before and during COVID-19 in Saudi Arabia, Int J Environ Res Publ Health, 18 (10) (2021), p. 5086
[48] M. Mesri, S.S. Esmaeili Saber, M. Godazi, et al. The effects of combination of Zingiber officinale and Echinacea on alleviation of clinical symptoms and hospitalization rate of suspected COVID-19 outpatients: a randomized controlled trial, J Compl Integr Med (2021), 10.1515/jcim-2020-0283
[49] O.E. Orisakwe, C.N. Orish, E.O. Nwanaforo, Coronavirus disease (COVID-19) and Africa: acclaimed home remedies, Sci Afr, 10 (2020), Article e00620
[50] S. F. Vesely, M. Nallappan, T. T. Tee et al., "Xanthorrhizol: a review of its pharmacological activities and anticancer properties," *Cancer Cell International*, vol. 15, no. 100, pp. 1–15, 2015.
[51] C. Maldonado, C. J. Barnes, C. Cornett et al., "Phylogeny predicts the quantity of antimalarial alkaloids within the iconic yellow *Cinchona* bark (Rubiaceae: *Cinchona calisaya*)," *Frontiers in Plant Science*, vol. 8, pp. 1–16, 2017.
[52] E. Abolghasemi, S. H. Moosa-Kazemi, M. Davoudi, A. Reisi, and M. T. Satvat, "Comparative study of chloroquine and quinine on malaria rodents and their effects on the mouse testis," *Asian Pacific Journal of Tropical Biomedicine*, vol. 2, no. 4, pp. 311–314, 2012.
[53] S. D'alessandro, D. Scaccabarozzi, L. Signorini et al., "The use of antimalarial drugs against viral infection," *Microorganisms*, vol. 8, no. 85, pp. 1–26, 2020.
[54] M. J. Vincent, E. Bergeron, S. Benjannet et al., "Chloroquine is a potent inhibitor of SARS coronavirus infection and spread," *Virology Journal*, vol. 2, no. 69, pp. 1–10, 2005.
[55] M.-B. Kim, C. Kim, Y. Song, and J.-K. Hwang, "Antihyperglycemic and anti-inflammatory effects of standardized *Curcuma xanthorrhiza* Roxb. extract and its active compound xanthorrhizol in high-fat diet-induced obese mice," *Evidence-Based Complementary and Alternative Medicine*, vol. 2014, Article ID 205915, 10 pages, 2014.
[56] C. Singgih Wahono, C. Diah Setyorini, H. Kalim, N. Nurdiana, and K. Handono, "Effect of *Curcuma xanthorrhiza* supplementation on systemic lupus erythematosus patients with hypovitamin D which were given vitamin D_3 towards disease activity (SLEDAI), IL-6, and TGF-β1 serum," *International Journal of Rheumatology*, vol. 2017, Article ID 7687053, 8 pages, 2017.
[57] Rhea Veda Nugraha, Hastono Ridwansyah, Mohammad Ghozali, Astrid Feinisa Khairani, Nur Atik,"Traditional Herbal Medicine Candidates as Complementary Treatments for COVID-19: A Review of Their Mechanisms, Pros and Cons", Evidence-Based Complementary and Alternative Medicine, vol. 2020, Article ID 2560645, 12 pages, 2020.

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